view that the modifications in treatment since 1936 have increased the chances of success both in suitable and in unfavourable eyes.

Maintenance of Improvement after Corneal Grafting

Perhaps one can best obtain the facts necessary to estimate the chances of maintaining the results of corneal grafting by considering the thirty-two eyes operated on up to 1936 and then reported. The patients were operated on in the period between seven and a half and two years ago. Two died before 1936, and in the case of the remaining thirty, seven grafts are now classified under a new result grouping. Three out of four eyes (Suitability Group A) show deterioration to a lower result group: one from Result Group 1 to Group 2 and two from Group 2 to Group 3. The fourth eye showed improvement from Group 3 to Group 2. Three eyes (Suitability Group B) showed deterioration: one from Result Group 2 to Group 4, one from Group 3 to Group 4, and one from Group 4 to Group 6.

These figures show that out of thirty grafts one improved and six deteriorated, while twenty-three remained as before over a period of some years. Seventeen of the thirty grafts were recorded as successes in 1936, and now, after a period of years, 14 are still so recorded. It is of interest to note that the patient whose graft improved was a case of interstitial keratitis, and the patient whose eye had to be removed owing to ulceration, a long time after the graft operation, was a very intractable young child who was able to give her eye very little fair treatment. One of the patients whose graft deteriorated from Result Group 2 to Result Group 3 is well known to our president, Sir Stewart Duke-Elder, and there were perhaps a few special reasons to account for the deterioration, such as chronic conjunctivitis and a tendency to recurring ulceration. There was also the common factor in these cases done before 1936 that oil was used for the reception of the graft, and probably it contributed to the deterioration in this patient's graft. The eye was regrafted six months ago, and the result grouping has thereby been raised from Group 3 to Group 2.

Summary

In the whole series of cases 62.5 per cent. of the operations and 66.6 per cent. of the eyes operated on were successes. The nine cases of interstitial keratitis were all successes, five of them exhibiting grafts that were clinically transparent. Operations on favourable cases showed 92 per cent. successful.

The results of cases operated on since 1936 by the modified technique show 80 per cent. of the operations successful, while the nine classified as favourable cases were all successful, and four of them had clinically transparent grafts.

The latter group of figures show improvement on the 1936 results, as do the results of the four regrafting operations, three of them being beneficial. While it is a fact that some grafts will fail to maintain the initial degree of transparency, this paper shows that in a series of thirty corneal grafts observed over a period of years one actually improved and six deteriorated. Three of these were in favourable cases, and although they deteriorated were still successful. The other three were in unfavourable cases. It is anticipated that with the modified technique now used the deterioration of 20 per cent. of the grafts over a period of years will be considerably reduced. At any rate, of those done before 1936 80 per cent. maintained their improvement.

In conclusion it is of interest to note that my best visual result is 6/9, and there are others with 6/12 vision, so that it is quite possible to obtain practically normal vision after corneal transplantation. One of my patients recently read four novels in ten days while on a voyage—two years after her operation.

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VITAMIN C IN THE TREATMENT OF WHOOPING-COUGH

BY

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The introduction of an effective treatment for whooping-cough is a matter of no little importance, since this disease now causes more deaths in this country than does any other infectious fever (Harries, 1938).

It seems true to say that although "nearly every newly discovered remedy in ancient and modern times has at one time been advocated for treatment of this disease" (Abt, 1937), there is not one that has been proved to have an appreciable effect on its course. Of vaccine or endotoxin therapy, lately so enthusiastically recommended, the conclusion of such an authority as Harries "that the more carefully the results are controlled the less impressive do they become" seems inescapable in the light of recent reports (Begg and Coveney, 1936; A. R. Thompson, 1937).

Earlier Experiences with Ascorbic Acid

The use of vitamin C or ascorbic acid as a remedy for whooping-cough was first reported by Otani (1936) from Tokyo. He found that ascorbic acid when added to a solid medium on which *H. pertussis* was grown inhibited the growth of that organism. The organism so cultured had impaired virulence when injected into rabbits. (Apparently these results were not controlled by substituting for ascorbic acid some other substance having a similar powerful reducing action.) Grootton and Bezssonoff (1936) also found that ascorbic acid in concentrations as small as 0.008 per cent. inhibited the growth of *H. pertussis* in culture media, whereas it had no such effect upon other organisms at concentrations up to 0.5 per cent. Acetic acid in similar amounts was found to be inert. Otani also found that in the presence of ascorbic acid the intradermal injection of *H. pertussis* toxin produced a diminished reaction in the rabbit: this effect was noted either when the ascorbic acid was mixed with the toxin or when the animal received a previous large dose of the acid. From these experiments Otani concluded that ascorbic acid specifically antagonizes the growth of *H. pertussis* and also inactivates its toxin. Scant details are given of the results of treatment of eighty-one patients with whooping-cough who were given intravenous or intramuscular injections of 50 to 200 mg. of ascorbic acid every two to three days; sixty-six of these were thought to be improved and fifteen unaffected. Results were better when treatment was started within the first week of the paroxysmal stage.

Ormerod and UnKauf (1937) of Winnipeg independently reported favourable results with ascorbic acid. They showed that "unsaturation" with ascorbic acid was common in cases of whooping-cough, a fact which was suggested also by the observation of Woringer and Sala (1928) of four cases of scurvy developing in the course of the disease. Using the urinary excretion method of assessing ascorbic acid saturation they worked out a standard dosage sufficient to saturate every case within a few days, irrespective of age or weight, and to maintain saturation throughout the course of the disease. Twenty-seven patients so treated were described: twenty-two were children whose symptoms had been present less than three weeks—that is, cases comparable with my series. The average duration of symptoms was nine days before and a further fourteen days after treatment was started, giving twenty-three days as the average course of the disease—a figure which is decidedly below that usually found in this country. There were no controls in this series.

The Present Series

This communication gives the result of treatment of forty-one children with whooping-cough, twenty-one of whom were treated solely with large doses of vitamin C, and twenty served as controls. They were seen as out-patients once a week; they became "treated" or "control" cases according to the day of the week on which they were first seen. Only those cases are included in this series which satisfied one or more (in the majority at least two) of the following diagnostic criteria:

1. *H. pertussis* recovered from cough plate.
2. A typical paroxysmal cough witnessed.
3. A suggestive history combined with the presence of *either* a sublingual ulcer *or* a marked lymphocytosis.

Only those whose cough was of less than three weeks' duration when first seen are included. The mothers were asked to note down on a form the number of paroxysms occurring during each separate day and each night, thus making the assessment of progress and of cure as objective as possible. In this way there was little need to rely on the parents' impressions as to whether the child was better or not. When the night cough had entirely ceased and the day cough was either absent or, if present, was stated to be quite slight and lacking a paroxysmal character, the patient was discharged. Each child was also weighed weekly, for in a disease where vomiting and loss of appetite are often prominent symptoms the child's weight chart was found to be a valuable guide to progress.

The Dosage Used

Conditions precluded any urinary or other estimations; therefore the policy was adopted of giving each "treated" child very large doses of vitamin C. The results of Ormerod and UnKauf were utilized when deciding on a standard dosage which was sufficient to ensure the rapid attainment and maintenance of "saturation." The dosage adopted was: first week, 200 mg. daily; second week, 150 mg. daily; third and subsequent weeks, 100 mg. daily, given in divided doses. This dosage was independent of age or weight except that patients under 1 year were given half these amounts. (These doses compare with 25 mg., the approximate daily requirements of the normal child.) The total weekly dosage is almost the same as that found necessary by Ormerod and UnKauf to ensure "saturation," and is considerably more than that employed by Otani. The form of ascorbic acid generally used was "ceetamin," a concentrate from natural sources; this was preferred to the synthetic product in view of the possibility that the latter is not identical in action with the naturally occurring vitamin (Elmby and Warburg, 1937). A few of the younger children received the synthetic acid (redoxon) as its smaller bulk was occasionally an advantage.

The controls were given cod-liver oil (15 per cent.) in malt in doses up to 1½ oz. daily, depending on age, and a mixture containing belladonna and bromide—drugs which are generally admitted to be without effect upon the duration of the disease (T. Thompson, 1929).

Results

The comparative results were as follows:

	"Treated"	Controls
Number of cases	21	20
Average age	2 yrs. 11 mos.	3 yrs. 4 mos.
Average duration of symptoms before treatment	10 days	14 days
Average duration of symptoms after treatment	25 ,,	27 ,,
Average total duration of illness	35 ,,	41 ,,
Average total weight gained during treatment	0.79 lb.	0.78 lb.
Average weight gained per week during treatment	0.22 lb.	0.20 lb.

The number of cases which were lost sight of before they had been discharged amounted to about 20 per cent. of the total, but as there was no appreciable difference between the number or type of cases lost from the "treated" and from the control series, it is considered legitimate to ignore this factor.

Complications.—The apparent incidence of complications is valueless where every case is not followed up, for it is just those cases which develop complications that may fail to report. Of the two cases of bronchopneumonia which are known to have occurred one was in the "treated" series (where it proved fatal) and one in the control series. These two cases are not included in the above results.

Summary and Conclusions

Twenty-one cases of whooping-cough have been treated with large doses of vitamin C. The illness lasted an average of thirty-five days, compared with forty-one days in twenty control cases, a difference which lies within the limits of statistical error.

The average rate of weight gained was practically the same in both the "treated" and the control cases.

These figures are in keeping with the general clinical impression that there was no striking difference in the course of the disease in the two sets of cases, and the assertion of Ormerod and UnKauf that the paroxysmal period of the disease is shortened "from a matter of weeks to a matter of days" was not confirmed.

In comparing these results with those of Ormerod and UnKauf it is seen that the average course of the disease in the cases treated with vitamin C was thirty-five days in the present series as compared with only twenty-three days in the Canadian series. The two sets of cases appear to be comparable in so far as the average period for which symptoms had existed before treatment was prac-

tically the same in both series. As there were no controls in the Canadian series, however, it is impossible to judge whether the natural course of the untreated disease varies in the two countries, or whether the considerable difference in the course of the disease in the present and in the Canadian series is due, for instance, to the application of a more rigorous standard of cure in the former series.

It is considered that the statement that the administration of vitamin C in whooping-cough has an effect upon the course of the disease is at present unproven.

My thanks are due to Dr. Donald Paterson for permission to publish these results relating to patients under his care and for his enthusiastic encouragement, to Dr. D. N. Nabarro for the haematological work, and to Dr. D. B. Bradshaw for the bacteriological work. Generous supplies of vitamin C preparations were given by Messrs. C. L. Bencard and by Messrs. Roche Products Limited.

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Clinical Memoranda

Recent Experience in Typhoid Fever

The following notes may prove interesting in connexion with the leading article in the *Journal* of May 21, and the papers by Fenton, Hay, and Felix in the same issue. An aberrant case of typhoid fever occurred in a small boarding house.

The patient, a commercial traveller, was infected while going his rounds in the West of England. He admitted feeling out of sorts for a week before December 1, 1937, when his illness started abruptly with fever and pain in the right side. Commencing pneumonia was diagnosed, but four days later typhoid was suspected on account of abdominal symptoms, including the passage of blood per rectum. Incidentally there was a history of gastric ulcer five years previously. At this time blood culture together with examination of faeces and urine and the Widal reaction were negative, nor was there leucopenia. A blood count on December 11 showed a slight relative and absolute increase of polymorphs, but a further Widal test on the same date was now strongly positive for *B. typhosus* (*B. typhosus* H = agglutination up to 1 in 2,500, and *B. typhosus* O = agglutination up to 1 in 1,000).

The patient was admitted to hospital on December 11 and died on December 23 from toxaemia and respiratory failure. On admission he was obviously very ill. He was delirious, his tongue was very dirty, there were signs of recent epistaxis, and he had a slight cough and was passing blood per rectum. The abdomen was moderately distended, with gurgling in the right iliac fossa. The spleen was not palpable, but there was tenderness in that region. A few rose spots were present on the lower costal margins and one to the right of the umbilicus. Although he gave a history of not more than twelve days' illness he was clinically in the third week. In addition to general treatment he received intramuscular injections of Lister Institute typhoid serum of 30 c.cm. each on December 14, 15, and 16 without any apparent benefit.

While in the boarding-house the patient was nursed by the owner's wife, who also prepared food for other residents, one of whom was a baker in a large establishment. It seemed likely that some of the household would be infected, and, apart from taking the baker off his work, the problem was what other steps were indicated.

We decided, with their consent, to give each of the six persons in the house 12 c.cm. of Lister Institute serum in order to produce, if possible, some degree of temporary passive immunity. A week and also a fortnight later this was followed up with the usual doses of T.A.B. vaccine (Lister Institute) with a view to producing active and more permanent immunity. We believe that there is a real danger of "provocation typhoid" if vaccine is used alone in such circumstances, and we suggest that pretreatment with serum is logical, and may possibly be sufficient in itself. No secondary cases occurred and no ill effects followed the inoculations. The sixth member of the household was a temporary visitor and had serum only so far as we know. Unfortunately circumstances were not favourable for subsequent blood examinations of the contacts, but one of us is able to vouch for the efficiency of the vaccine from controls taken elsewhere.

Regarding sulphonamide in enteric fever, one of us has tried this drug by the mouth in one case of typhoid and in several of paratyphoid B. In the latter it appeared to have a favourable effect, but it must be admitted that cases of this disease which come under treatment early often run a mild course. The single case of typhoid was a severe one, but recovered eventually. The drug had no effect one way or the other, and as the patient was found to be a temporary urinary carrier in convalescence and was a chronic faecal carrier on discharge, it would appear that sulphonamide has no bactericidal properties in typhoid fever.

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Ether Convulsions, with Recovery

The use of evipan in ether convulsions was first described by R. F. Woolmer and one of us (S. T.) in 1936. Its value was independently discovered by J. S. Marr (1936), and one month later T. H. Chadwick (1936) reported his case. Dr. H. H. Pinkerton's recent account of the successful treatment of ether convulsions with evipan in the *Journal* (1938) prompts us to record two similar cases.

Case Records

Case 1.—A child aged 4 years was undergoing operation for double mastoid suppuration. The anaesthetic was ethyl chloride, followed by open ether, then by ether vaporized with oxygen. When anaesthesia had been in progress for sixty minutes, and as the operation on the second ear was starting, typical ether convulsions began. The convulsions were unrelieved by oxygen and CO_2 and the removal of the clothes. Evipan was then injected intravenously, and when 8 c.cm. had been given the convulsions ceased. So too did respiration, and after half a minute of CO_2 and artificial respiration the pulse also stopped. Coramine, 1.5 c.cm., was then injected into the heart, and within a few seconds pulsation started once more. Artificial respiration was continued, and three minutes later spontaneous respiration began. The respirations increased in volume, and the child made a complete recovery. The operation on the second ear, however, was temporarily abandoned. The theatre temperature was 80° F., and the rectal temperature, after five minutes with no clothes on, was 101.5° F. The ether contained traces of aldehyde, but no peroxide. Two days later the second operation was performed, with the same anaesthetic, but paraldehyde ʒ iiss was given beforehand. There was no recurrence of the convulsions.